UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,449	11/22/2006	Luc Bouwens	BOUW3001/JEK	8208

23364 7590 10/07/2008

BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314-1176

EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
10/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,449	BOUWENS ET AL.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-61* is/are pending in the application.

4a) Of the above claim(s) *57-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-56 and 61* is/are rejected.

7)☒ Claim(s) *51 and 61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/2007 03/12/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of claims 45-56 and 61 in the reply filed on 06/30/2008 is acknowledged.

2. Claims 57-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/30/2008.

3. Claims 45-56 and 61 are under consideration.

Claim Objections

4. Claim 61 is objected to because of the following informalities: Claim 61 has a grammatically incorrect singular article referring to a plural object: **a** dedifferentiated mammalian pancreatic **cells**. Appropriate correction is required.

5. Claim 51 is objected to because of the following informalities: The expression "depleting said population from beta cells" is syntactically awkward in standard English. It is interpreted as "depleting beta cells from said population". Unless a different meaning is intended, correction is recommended.

Claim Rejections - 35 USC §101 and 112

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 61 is drawn to a population of mammalian pancreatic cells according to claim 52 being identifiable by an in vitro method for determining the degree of redifferentiation of dedifferentiated mammalian pancreatic cells comprising the steps of determining one or more parameters. The claim appears to recite both a product (cell population) and a process for identifying cells, but it is not clearly a product-by-process claim. The process is not complete as it recites parameters to be determined, but does not indicate how the determinations identify the cells. All cells are "identifiable" by performing the recited determinations, no specific outcomes are required.

9. Claim 61 is rejected under 35 U.S.C. 101 because the claim is directed to neither a "process" nor a "composition of matter", but rather embraces or overlaps two different statutory classes of invention set forth in 35 U.S.C. 101, which is drafted so as to set forth the statutory classes of invention in the alternative only *Ex parte Lyell*, 17 USPQ2d 1551 (Bd. Pat. App. & Inter. 1990).

10. Claim 55 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 55 recites "RPMI-1640 medium supplemented with 10% fetal bovine".

Although one of skill in the art would expect that the intent is to recite fetal bovine *serum*, in the absence of this specific recitation, the claim is indefinite.

11. Claim 55 is further indefinite as it recites "being able to provide an insulin secretion of at least 10 ng/ml". Cells that produce any amount of insulin in response to glucose could easily secrete 10 ng/ml if they were placed in a small enough volume of medium. Conversely, cells that produce a large amount of insulin could be made to look as if they had failed to produce 10 ng/ml if they were placed in a large enough volume of medium. It is therefore unclear how this recitation further limits the base claim.

12. Claims 45-46 and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All claims are dependent from claims 45 or 52, which recite "adding one or more ligands of the gp130 receptor of a second mammal and/or adding one or more ligands of the EGF receptor of a third mammal to said culture medium". In the embodiment wherein the 'or' option is chosen and only a ligand of the EGF receptor is to be added, "third mammal" is undefined, as there would be no "second mammal".

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 45-48, 50, 52 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20060122104 (Presnell), filed May 22, 2003, with a claim of priority to May 28, 2002. The instant claims are drawn to methods of generating insulin producing beta cells from a population comprising dedifferentiated exocrine pancreatic cells comprising incubating the cells in medium containing one or more ligands of the gp130 receptor of a second mammal and/or one or more ligands of the EGF receptor of a third mammal.

15. Presnell teaches methods for in vitro expansion and transdifferentiation of human pancreatic acinar cells into insulin-producing cells (whole document; see title). In the disclosed procedure, primary pancreatic acinar cells (as in claim 50) were collected as waste from a procedure prepare islet cells, which would deplete beta cells, as recited in instant claim 51. The cells are placed in culture, wherein they initially display ductal and acinar markers, and subsequently acquire a modified phenotype, termed "intermediate progenitor" (IP) [0009]. IP cells are equivalent to the "dedifferentiated exocrine pancreatic cells of the instant claims; for example, they express CK7 and CK19, recited in instant claim 61 [0009]. The cells can undergo additional steps of differentiation in vitro, culminating in the formation of cell aggregates that express pro-insulin and C-peptide, and which secrete insulin in response to a glucose challenge [0011]. The population of insulin producing cells disclosed in Prenell is indistinguishable from the populations recited in instant claims 52 and 61 (see [0033]). EGF, TGFα, betacellulin (EGF receptor ligands), LIF (a gp130 ligand recited in instant claim 46) and bFGF, which is recited in instant claim 48, are identified as a useful for promoting the expansion, transdifferentiation, and differentiation of pancreatic cells, ([0015, 0027]. A finite list of preferred factors to be used alone or in combination to promote differentiation of cultured pancreatic acinar cells into insulin-

producing cells, which includes TGFα, LIF, and FGF1, but lacks gastrin or KGF (see instant claims 49), is disclosed in Table 1 ([0027], see also [0093]).

16. Presnell practiced the method using media that comprised LIF or both LIF and TGFα, (combinations 2 and 3, respectively; see [0093]) thereby meeting the each of conditions recited as "and/or" in independent claims 46 and 52. Cells differentiated in either condition exhibited at least two-fold increase in insulin secretion upon glucose challenge with either 5 mM or 22 mM glucose (Fig. 14). Presnell does not teach, however, the same conditions for performing the glucose challenge as recited in instant claims 54 and 55 (18 hours in either 5 or 22 mM glucose (Presnell at [0102]) as opposed to 4 hours in 20 mM glucose). Presnell's results, however, indicate that different growth factor compositions of the differentiation medium can result in populations with different stimulated insulin secretion (see Figs. 14 and 15). Therefore, even if the respective responses to glucose challenges are not inherently the same (a realistic possibility, given the higher extent of stimulated insulin secretion in Presnell (see Figs. 14 and 15)), the presently claimed results would be obtained by routine optimization based on the teachings in Presnell.

17. Presnell does not teach that the sources of ligands of the gp130 receptor or EGF receptor should be of a second mammal or a third mammal, relative to the source of cells in a first mammal, as recited in the instant claims. Presnell does not generally indicate the species sources for the numerous growth factors mentioned and used in that specification. This reflects the implicit understanding that ligand-receptor pairs are highly conserved such that factors from any mammalian species would be expected effectively bind and activate the corresponding receptors from most other mammalian species. The instant specification teaches that "EGF, LIF and other

compounds used in the methods of the present invention for the redifferentiation can be from the same species but can also be from another species as long as the compound can bind and activate its receptor" ([0040] in the published application). Thus, the instant specification acknowledges the expected functional equivalence of growth factors from mammalian species, and explicitly teaches that the source of growth factor is not critical to the practice of the claimed methods. No unexpected results are disclosed regarding the source of growth factors. Therefore, in view of Presnell, the instant limitations reciting "of a second mammal" (or "third mammal") represent a simple substitution of one known element for another to obtain predictable results. One of skill in the art would expect to perform the claimed methods using cells and factors entirely from a single species and obtain the same results as claimed. (It is noted that such practice would not literally infringe the instant claims). The Supreme Court reaffirmed principles, based on its precedent, that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR International Co. v. Teleflex Inc. (KSR), 550 U.S.___at, 82 USPQ2d at 1395.

18. Claims 45, 47, 50-52, 55, 56 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable US Patent 6,815,203, filed June 23, 2000. The '203 patent discloses methods for "dedifferentiation" of pancreatic cells, which can then "redifferentiate" into insulin-producing islet cells (column 1, lines 44-60). Specifically, the methods of the '203 patent involve isolation of pancreatic tissue depleted of islets (thereby depleting beta cells, as in instant claim 51; see column 27, lines 27-50; see also claims 1 and 12) and culturing exocrine pancreatic cells (i.e. acinar cells) in conditions that promote "dedifferentiation" into an intermediate cell type that is

capable of subsequent differentiation into an insulin-producing cell. The dedifferentiated pancreatic cells in the '203 patent express CK19 (column 5, lines 37-40; column 30, lines 31-50), which is disclosed as a marker of dedifferentiated cells in the instant application (see [0015] of the published instant application). Thus the starting population of cells in the '203 patent is the same as disclosed in the instant specification and recited in instant claims 46 and 52. The '203 patent further discloses differentiation of dedifferentiated cells in the presence of EGF (see claim 23), as recited in instant claims 45, 47, and 52. Thus, the '203 patent discloses the same instantly claimed process, which would necessarily yield an insulin-producing cell product cell population that is indistinguishable from that recited in instant claims 52-55, and 61. This is supported by increases in expression of insulin and observation of glucose-stimulated insulin secretion (column 32, lines 14-59). The '203 patent teaches therapeutic administration of the differentiated cells in as pharmaceutically acceptable carrier (column 27, lines 24-25) as recited in instant claim 56.

19. The '203 patent does not teach that the source of ligand of EGF receptor should be "of a second mammal or a third mammal", relative to the source of cells in a first mammal, as recited in the instant claims. This distinction, however, is obvious for reasons explained fully above in the rejection of these same claims under 35 U.S.C. 103(a) as being unpatentable over US 20060122104 (Presnell).

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel C Gamett/
Examiner, Art Unit 1647